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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08 989,896	12 12 1997	MATHIAS GEHRMANN	05552.1337-0	9415

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EXAMINER

SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
1644	27

DATE MAILED: 11/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	984,896	Applicant(s)	GERMAN et al
Examiner	SAUNDERS	Group Art Unit	1647

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

Responsive to communication(s) filed on 7/12/02
 This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

Claim(s) 1-22, 25-33 is/are pending in the application.
 Of the above claim(s) 1-14-22 is/are withdrawn from consideration.
 Claim(s) _____ is/are allowed.
 Claim(s) 1-13, 25-33 is/are rejected.
 Claim(s) _____ is/are objected to.
 Claim(s) _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
 The proposed drawing correction, filed on _____ is approved disapproved.
 The drawing(s) filed on _____ is/are objected to by the Examiner.
 The specification is objected to by the Examiner.
 The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 All Some* None of the CERTIFIED copies of the priority documents have been received.
 received in Application No. (Series Code/Serial Number) _____
 received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Attachment(s)

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ Interview Summary, PTO-413
 Notice of Reference(s) Cited, PTO-892 Notice of Informal Patent Application, PTO-152
 Notice of Draftsperson's Patent Drawing Review, PTO-948 Other _____

Office Action Summary

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The claims pending are 1-22 and 25-33. The claims under examination are 1-13 and 25-33.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's amendment (filed 7/12/02) of claim 1 has overcome the previously stated 112, first paragraph, new matter rejection.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant has not shown that the L6 hybridoma was publically available as of the filing date.

Applicant has urged that the exhibit of the PNAS online Information for authors overcomes the rejection of record. It does not for the following reasons:

- 1) The information was revised as of May 2002. There is no evidence on the record as to whether the Journal Policies, set forth in part (vii) regarding the availability of materials were in effect at the time of filing. Required materials must be publically available as of the filing date. ¹⁰⁴ *Ex parte Moersch USPQ 122.*
- 2) The Journal Policies merely require that antibodies be provided, while 37 CFR 1.801-1.809 require that a replicable material, i.e., the hybridoma cells secreting the antibody, be made publically available.

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Applicant's amendment and urgings filed on 7/12/02 are convincing that the 112, first paragraph, scope of enablement rejection, with respect to the nature of the linkers, should be withdrawn.

Applicant's amendment has necessitated the following new 112 rejection.

Claims 1-13 and 25-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing in that parts a) and b) refer to the claimed compound as "a polypeptide chain", while part c) refers to a "nucleotide sequence". As such, part c) cannot be properly recited as being a component /feature of the claimed compound.

The following rejections of record are maintained.

Claims 1-9, 25-27, 30 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosslet et al. (Brit J. Can. 65,235, 1992) or Seemann et al. (EP 0,501,215 or CA 2,062,047) in view of Huston et al. (5,132,405) and, as necessary Bosslet et al. (EPO 040,097 or U.S. 5,591,828) and Eaton et al. (EP 0,392,745).

Claims 1-2, 9, 11-12 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosslet et al. or Seemann et al. in view of Huston et al. and, as necessary, Bosslet et al. and Eaton et al. as applied to claims 1, 10, 13 and 29 are above, and further in view of Ong et al. (Can Res., 51, 619, 1991), Bagshawe et al. (WO 89/10140) and Huston et al; (Meth. Enz, 204, 46, 1991).

Claims 1, 10, 13 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosslet et al. or Seemann et al. in view of Huston et al. and, as necessary, Bosslet et al., Bagshawe et al. and Huston et al. as applied to claims 1, 9, 11-12 and 31-32 above, and further in view of Gooch et al. (Biotechnol, 9, 1347, 1991).

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Claims 1, 6 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosslet et al. or Seemann et al. in view of Huston et al. and, as necessary, Bosslet et al. and Eaton et al. as applied to claim 1 above, and further in view of Bayshawe et al. (WO 88/07378).

Applicant has urged that it is improper for the examiner to make an obviousness rejection, given that he has made a 112 rejection on the grounds of undue experimentation. Irrespective of whether or not this is proper, the argument is moot, since the examiner has withdrawn the 112 rejection of record.

Applicant has urged that since the instant disclosure teaches chemical linking as well as fusion of sFv to an enzyme, one would not have envisioned the enzyme being encoded by the same strand encoding the antigen binding domain. The examiner considers that Huston et al.'s teaching that the sFv may be fused to an enzyme is sufficient, since by the well understood definition of a fusion polypeptide such a polypeptide is encoded by a single strand of nucleic acid which has been formed by joining two segments encoding polypeptide domains having the same or differing functions. Applicant cannot rely upon alternative teachings within his own specification to argue that the prior art taught away from fused polypeptides.

Applicant has urged that since only Huston et al. teach sFv constructs and since Seemann et al. and Bosslet teach that "their constructs should be made so that the tumor binding portion should be as similar as possible to the original antibody" that the art was "undecided" as to how to generate such constructs. This argument merely argues the reference of Huston et al. separately from those of Seemann et al. and Bosslet et al. Applicant has not shown that there was

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any state of “uncertainty” or “existing confusion” in the literature as to whether Fab or sFv constructs should be used. Furthermore, whether or not Huston et al.’s teachings “follow the majority thinking in the field” is not relevant to overcoming obviousness because this argues the teachings of Huston et al. in isolation from the combination of references.

In response to applicant’s arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant has further urged that there is no motivation to combine the teachings of the references, and then has not argued the point except by the false argument (as noted above) that Seemann and Bosslet et al. teach away from the claimed invention.

Applicant has then argued that the Office is in error that the claimed invention does not include constant region sequences. Applicant merely points to specification Example 3. The examiner fails to see how any of the features of Example 3 have been necessarily incorporated into the claims, as amended on 7/12/02.

Applicant has urged that the Office has relied upon “general conclusions” about knowledge in the art. The examiner has merely relied upon well known scientific knowledge in the pertinent field of knowledge and has not followed any line of unstated reasoning to arrive at these. The obviousness rejections of record are therefore proper and not in conflict with *In re Lee*.

Claims 1-4, 8-9, 25-26 and 33 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Winter et al (6,248,516), for reasons of record.

Claims 1-2, 4-5, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winter et al (6,248,516) in view of Seemann et al, for reasons of record.

Claims 1, 6, 27, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winter et al (6,248,516) in view of Eaton et al, for reasons of record.

Claims 1, 6 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winter et al (6,248,516) in view of Bagshawe et al (WO 88/07378), for reasons of record.

Claims 1-2, 9, 11-12 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winter et al (6,248,516) in view of Ong et al and Bagshawe et al (WO 89/10140), for reasons of record.

Claims 1, 10, 13 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winter et al (6,248,516) in view of Ong et al and Bagshawe et al (WO 89/10140) as applied to claims 1-2, 9, 11-12 and 31-32 above, and further in view of Goochee et al, for reasons of record.

Applicant has traversed all rejections based upon Winter et al with the argument that language introduced into claim 1, parts b) and c), concerning the "polypeptide linker" and the process by which this is formed as a link between the first and second variable domains, overcomes Winter et al. The teachings of Winter et al have not been overcome because what is being claimed is a polypeptide product having a polypeptide linker therein. No weight is given, therefore, to any process as recited in part c) by which the polypeptide linker might have been inserted. All that is required is that the prior art teach a linking polypeptide, irrespective of the

process by which it might have been inserted in the polypeptide chain. Winter et al clearly teach linking peptides/polypeptides between two variable domains of a single chain antibody (e.g. col. 13, lines 52-54).

Applicant's urgings of 7/12/02 have been considered but are unconvincing of patentability.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday from 8:00 a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

October 30, 2002

David A. Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
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